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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,304	04/20/2007	Naoki Kimura	14875-166US1 CI-A0323P-US	4817

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EXAMINER	
GUSSOW, ANNE	

ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
09/15/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/582,304	KIMURA ET AL.	
	Examiner	Art Unit	
	ANNE M. GUSSOW	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,17-24 and 29-46* is/are pending in the application.

4a) Of the above claim(s) *17-21,29-31 and 35-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,22-24 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/30/09, 8/10/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 21-24 have been amended.

Claims 11-16 and 25-28 have been cancelled.

Claims 29-46 have been added.

Claims 17-21 remain withdrawn and newly added claims 29-31 and 35-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on December 16, 2008.

2. Claims 1-10, 22-24, and 32-34 are under examination.

3. The following office action contains NEW GROUNDS of Rejection.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on June 30, 2009 and August 10, 2009 were filed after the mailing date of the first action on the merits on April 1, 2009. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner and an initialed copy of the IDS is included with the mailing of this office action.

Objections Withdrawn

5. The objection to the specification is withdrawn in view of applicant's amendment to the specification.

6. The objection to the title is withdrawn in view of applicant's amendment to the title. The new title is "Single chain polypeptide antibodies that bind human leukocyte antigen".

Rejections Withdrawn

7. The rejection of claim 16 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of applicant's cancellation of the claim.

8. The rejection of claim 16 under 35 U.S.C. 112, first paragraph, as lacking enablement is withdrawn in view of applicant's cancellation of the claim.

Rejections Maintained/ NEW GROUNDS of Rejection

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The rejection of claims 1-10, 22-24, and newly added claims 32-34 under 35 U.S.C. 103(a) as being obvious over Ozaki, et al. (Blood, 2003. Vol. 102, page 933a) in view of Kortt, et al. (Biomolecular Engineering, 2001. Vol. 18, pages 97-108) is maintained. The NEW REJECTION of claims 8-10 is addressed below, as evidenced by the specification.

Applicant's arguments filed June 30, 2009 have been carefully considered by the examiner but they are deemed not to be persuasive. The response states that Ozaki et al. teach a monoclonal antibody (2D7) as well as a single-chain Fv diabody (2D7-DB). Ozaki teaches that, while 2D7 induced cytotoxicity only in the presence of secondary goat anti-mouse IgG, 2D7-DB effectively cross-linked HLA-A and induced cell death by itself. In addition, 2D7-DB was found to have in vivo efficacy in SCID mice inoculated intravenously with myeloma cell line ARH-77. Kortt et al. describe the design and expression of diabodies (dimers), triabodies (trimers) and tetrabodies (tetramers) (see, title and abstract). This reference states: This review describes how the length of the linker joining the V-domains and selection of the V-domain orientation can be used to create new non-covalent oligomeric forms of Fv modules of different size, flexibility and increased valency suited for in vivo imaging and therapy. (see, page 96, left column, first full paragraph, second sentence). (emphasis supplied). In other words, Kortt is not directed to single chain sc(Fv)2 molecules as asserted by the Action (see, page 16, first and third paragraphs), but rather to non-covalent oligomers containing multiple chains (e.g., diabodies containing two chains, triabodies containing three chains and tetrabodies containing four chains). Even if there were some reason to modify Ozaki

with Kortt (which Applicants do not concede), the combination of Ozaki and Kortt would not teach all claim limitations, because neither reference teaches or suggests one should modify diabodies into sc(Fv)2 polypeptides. Instead of teaching the use of sc(Fv)2 molecules, Kortt is entirely directed at emphasizing the benefits of multi-chain, oligomeric forms of Fv modules, such as diabodies (see response pages 11-14).

In response to this argument, the examiner agrees that Kortt teaches a number of antibody molecules however, the relevant molecules to this discussion are at the bottom of page 95 and the top of page 96 where Kortt states:

> "Recent design variations of engineered antibodies have included reduction in size to single-chain Fvs, dissection into minimal binding fragments such as VH domains and rebuilding of scFvs into multivalent high-avidity oligomeric scFvs (Figure 1)"

In looking at Figure 1 the portion labeled “Bivalent ScFv fragments” is clearly an sc(Fv)2 because the linkers L1 and L3 join the portions of the scFv and the linker L2 joins the two svFv molecules in to a single chain. The discussion of the length of the linker in figure 3 is relevant to the sc(Fv)2 molecule because Kortt makes clear that the length of the linker is the portion of the molecule responsible for the structural folding and formation of the different antibody structures and Kortt provides several linkers in Figure 3 for the production of these antibodies. Further, Kortt discusses the multivalent molecules in figure 1 provide a significant increase in functional affinity (page 96 column 2.) Thus, the Kortt reference does not teach away from the instant claims as asserted by applicant, but rather provides information towards producing a number of different antibody structures.

Regarding the newly rejected claims 8-10, Ozaki, et al. teach a 2D7 antibody clone which binds to HLA and has a cell death inducing function, a cell growth inhibitory function, and an anti-myeloma (blood tumor) function. The specification discloses the 2D7 antibody clone was used to produce the sv(Fv)2 as instantly claimed (see page 2 lines 26-36). Thus, the sequence of the Ozaki, et al. antibody and the instantly claimed SEQ ID Nos. 3-8 would necessarily be identical.

Regarding the pharmaceutical composition of claims 22-24 and 32-34, the pharmaceutical composition is an intended use of the claimed antibody and as such receives no patentable weight.

Thus, for the reasons set forth above and in the previous office action one of ordinary skill in the art would be motivated to and have a reasonable expectation of success to have produced an sc(Fv)2 which maintained the cell death inducing, cell growth inhibiting and anti myeloma functions as taught by Ozaki, et al. in view of Kortt, et al.

Therefore after a fresh consideration of the claims and the evidence provided the rejection is maintained.

Conclusion

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is

(571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow
September 10, 2009

/Anne M Gussow/
Examiner, Art Unit 1643